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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1643	

NOTIFICATION DATE	DELIVERY MODE
10/17/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@kenyon.com

Office Action Summary	Application No.	Applicant(s)	
	10/720,273	HOLMGREN ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-33* is/are pending in the application.

4a) Of the above claim(s) *33* is/are withdrawn from consideration.

5)☒ Claim(s) *22 and 27* is/are allowed.

6)☒ Claim(s) *21,23-26 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant has timely traversed the non-final rejection in the reply filed on 07/23/2007, and a response to the arguments is set forth.

2. Claims 1-20 have been cancelled.

3. Claims 21-33 have been newly added.

4. Newly submitted claims, claim 21-33, are directed two separate inventions. Claims 21-32, Invention I, are drawn to an isolated antibody or antibody fragment; and Claim 33, Invention II, is drawn to a method for treating an angiogenesis related disease comprising administering an effective amount of an antibody

Thus, inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § 806.05(h)]. In the instant case the antibody product as claimed can be used in a materially different process such as affinity chromatography in addition to the materially different methods of claim 33.

Since the applicant has elected the Group corresponding to the product claims in response to the restriction/election mailed on 05/16/2006; the method claim, claim 33, is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

In response to the applicants reference to U.S. Patent 6,908,898 (page 7 of the response filed on 07/23/2007); the products were indeed indicated restricted from the

method claims in the parent case. However, upon the indication of the allowance of the product claims, the method claims were rejoined. Similarly, in the instant case, the applicant is reminded that once the product is found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Also, see MPEP § 821.04(b).

5. Claims 21-32 read on the elected invention and are under examination.

6. This office action consists of new grounds of rejections.

Please note that the art cited in the new grounds of rejections is of record in the PTO-892 mailed on 04/19/2007.

Objections Maintained

7. The objections of the disclosure is maintained because the first line of the specification is not updated to incorporate the U.S. Patent number of the parent application 09/332,063.

Rejections Withdrawn

8. All the rejections set forth in the previous office action, of claims 1-19, are withdrawn in view of cancellation of the claims.

New Grounds of Rejections

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 21, 23-26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one

skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

In the instant case, the claims are drawn to an isolated antibody or antibody fragment which specifically binds an isolated mammalian protein wherein said protein comprises an amino acid sequence having 80% sequence homology or greater to SEQ ID NOs:2, 3 or 4; an isolated antibody or antibody fragment to a peptide which has an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2; an isolated antibody or antibody fragment which specifically binds an isolated mammalian protein comprising an amino acid sequence encoded by a nucleic acid molecule that binds under stringent conditions to the nucleotide sequence from position 797-2824 or from position 2180-2606 of SEQ ID NO:1.

While the amino acid sequence of SEQ ID NOs:2, 3 and 4 is adequately described in the specification as-filed, thereby providing an adequate basis for the polypeptide of SEQ ID NOs:2, 3 and 4; there is insufficient written description as to the identity of a polypeptide having at least 80% sequence identity to SEQ ID NOs:2, 3 or 4 any peptide which has an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2 that would still maintain the function of the polypeptide. Consequently, the specification does not provide an adequate written description of an antibody to a polypeptide having at least 80% sequence identity to SEQ ID NOs:2, 3 or 4. The specification does not provide sufficient written description for all the amino acid sequences encoded by a nucleic acid molecule that binds under stringent conditions to the nucleotide sequence from position 797-2824 or from position 2180-2606 of SEQ ID NO:1; or any antibody that binds to all such amino acid sequences.

The specification as filed does not provide adequate written description support for an antibody to a polypeptide having at least 80% sequence identity to SEQ ID NOs:2, 3 or 4. Polypeptides having diverse functions are encompassed by the phrase 80% identity. For example, Alitalo et al (PGPUB 20060088532) teach a polypeptide as set forth in SEQ ID NO:249, that has a 95.1% identity to the instantly claimed SEQ ID NO:2, 99.5% identity to the instantly claimed SEQ ID NO:3 and 100% identity to the instantly claimed SEQ ID NO:4. Alitalo et al teach that such polypeptide and the related polypeptides are differentially expressed in the lymphatic endothelial cells which can be used as targets for tumor therapy (please see summary of the invention). Griffin et al (WO 200305023) teach human cell growth, differentiation and death (CGDD) protein that has 99.5% identity to the instantly claimed SEQ ID NO:2, 99.4% identity to the claimed SEQ ID NO:3 and 100% identity to the instantly claimed SEQ ID NO:4 (please see the sequence search results attached at the end of this office action for the % identity). These references show that the polypeptides that share as high as 94% homology to the instantly claimed proteins vary in functions. Thus a broad genus having potentially highly diverse functions is encompassed by the phrase 80% sequence identity and conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., Abstract and Sequence-based approaches to function

prediction, page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisans best guess as to the function of the structurally related protein (see in particular Abstract and Box 2). Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad genus. The instant claims are broadly generic to all possible proteins encompassed by the claims. The possible variations are enormous to any class of polypeptides. Since the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of SEQ ID NOs:2, 3 and 4 beyond those disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of such polypeptides as claimed.

While having written description of SEQ ID NOs:2, 3 and 4 identified in the paragraphs 38-43 of the specification, the specification is devoid of any other

polypeptides that qualify for the functional characteristics claimed. Further, while having the written description for the polypeptide encoded by the nucleotide sequence from position 797-2824 and from position 2180-2606 of SEQ ID NO:1, which are SEQ ID NOs:2 and 4, respectively (page 7 of the instant specification, in particular); the specification is devoid of any other polypeptides encoded by a nucleic acid molecule that binds under stringent conditions to the nucleotide sequence from position 797-2824 or from position 2180-2606 of SEQ ID NO:1; or any antibody that binds to all such amino acid sequences. The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Further, in reference to claim 25, wherein the claim is drawn to an antibody or antibody fragment to a peptide which has an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2, the specification teaches that the subfragment of SEQ ID NO:2 equivalent to SEQ ID NO:4 was isolated in a screening assay designed to isolate proteins which bind to the kringle domains present in the N-terminus of plasminogen, such as angiostatin. SEQ ID NO:4 is 143 amino acids in

length. The instant claim 25 encompasses a genus of peptides which minimally comprise 10 contiguous residues of SEQ ID NO:2 and wherein said peptide bind to an N-terminal fragment of plasminogen. The disclosure of SEQ ID NO:4 as binding to angiostatin does not adequately describe the claimed genus. The genus tolerates proteins which minimally comprise regions of SEQ ID NO:2 rather than SEQ ID NO:4, and further, the genus tolerates proteins wherein said proteins bind to "an" N-terminal fragment of plasminogen which is outside of the kringel domains of plasminogen. For example, members of the genus would include proteins which comprise 10 contiguous residues of SEQ ID NO:2 which bind to residues of plasminogen, but wherein binding of said proteins to plasminogen do not evoke an anti-angiogenic response.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any

of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed

correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of the peptides which minimally comprise 10 contiguous amino acids of SEQ ID NO:2 and which bind to the N-terminus of plasminogen, per Lilly by structurally describing a representative number of peptides having the characteristics claimed or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the peptides of claim 25 in a manner that satisfies either the Lilly or Enzo standards. The specification provides the complete structure of SEQ ID NO:4 as the only peptide which comprises at least 10 contiguous amino acids of SEQ ID NO:2. The specification does not provide any partial structure of such peptides, nor any physical or chemical characteristics of the peptides nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single peptide of

143 amino acids which, this does not provide a description of a genus of peptides that would satisfy the standard set out in Enzo.

The specification also fails to describe the peptides of claim 25 by the test set out in Lilly. The specification describes only a single peptide of SEQ ID NO:4. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus." It is noted that SEQ ID NO:4 is 143 amino acids in length and would bind to kringle domains 1-4 and/or 5. However, it is noted that SEQ ID NO:4 would not have anti-antiangiogenic activity as SEQ ID NO:4 would not have an intracellular domain for signal transduction.

Therefore, only SEQ ID NOs. 2, 3 and 4 meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed. (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Response to Applicants arguments:

The applicants argue that the claims are supported by the specification and that the specification discloses working examples that describe an assay for assessing the functions of the anti-angiogenic activity of a protein with 80% sequence homology or greater to SEQ ID NO:4 ... the antigens function is disclosed as a receptor of angiostatin that mediates angiogenesis (page 8 of the response filed on 07/23/2007). Applicants argue that given the teachings of the specification of both structural and functional features of anti-angiogenic proteins encompassed by the claims, a sufficient written description has been provided.

The above arguments are carefully considered but are not found persuasive. As stated above, the specification discloses SEQ ID NOs:2, 3 and 4 (paragraphs 38-43, in particular) and the polypeptides encoded by the nucleotide sequence from position 797-2824 and from position 2180-2606 of SEQ ID NO:1, which are SEQ ID NOs:2 and 4, respectively. The specification is completely silent as to all the peptide or protein molecules that are encompassed within the claims, much less the antibodies that bind to all such peptide or protein molecules. The specification does not disclose any polypeptide having at least 80% sequence identity to SEQ ID NOs:2, 3 or 4, any peptide which has an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2 or any amino acid sequences encoded by a nucleic acid

molecule that binds under stringent conditions to the nucleotide sequence from position 797-2824 or from position 2180-2606 of SEQ ID NO:1. A mere statement that the amino acid sequences encompassed within the claims are anti-angiogenic, and describing an assay for assessing the functions of the anti-angiogenic activity of a protein is not sufficient support for written description. Neither does it indicate to a skilled artisan that the applicant was in possession of all the embodiments that are encompassed within the claims.

The application does not provide any description to reasonably convey a skilled artisan that the applicant was in possession of the claimed invention at the date of invention (See also MPEP 2106). The application as filed neither discloses the complete structure of all the polypeptides having at least 80% sequence identity to SEQ ID NOs:2, 3 or 4, all the polypeptides that have an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2 and all the amino acid sequences encoded by a nucleic acid molecule that binds under stringent conditions to the nucleotide sequence from position 797-2824 or from position 2180-2606 of SEQ ID NO:1, nor discloses any relevant identifying characteristics sufficient to describe all such amino acid sequences in full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of all the embodiments encompassed within the claimed invention; much less antibodies to such amino acid sequences. Further, the art does not establish a strong correlation between structure and function of all such claimed amino acid sequences Hence, one skilled in the art would not be able to predict with a reasonable degree of confidence the structure of the claimed invention from a

recitation of its function. Thus, the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. In contrast, without such a correlation, the capability to recognize or understand the structure from the mere recitation of function and minimal structure is highly unlikely. In this latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406 (written description requirement not satisfied by merely providing "a result that one might achieve if one made that invention"); In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming a rejection for lack of written description because the specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Compare Fonar, 107 F.3d at 1549, 41 USPQ2d at 1805 (disclosure of software function adequate in that art).

11. Claims 21, 23-26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or antibody fragment which specifically binds to an isolated mammalian protein comprising an amino acid sequence as set forth in SEQ ID NOs: 2, 3 and 4, does not reasonably provide enablement for an antibody or antibody fragment which specifically binds an isolated mammalian protein comprising an amino acid sequence having at least 80% sequence homology to SEQ ID NOs: 2, 3 or 4. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The claims have been described supra. Thus the claims are broadly drawn to an antibody that binds to a polypeptide comprising at least 80% sequence homology to SEQ ID NOs:2, 3 and 4, an antibody that binds to a peptide that has an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2 and an antibody that binds to polypeptides encoded by a nucleic acid molecule that binds under stringent conditions to the nucleotide sequence from position 797-2824 or from position 2180-2606 of SEQ ID NO:1.

The specification teaches amino acid sequence 2, 3 and 4 and the antibodies that bind to such amino acid sequences, in addition to that the polypeptides encoded by the nucleotide sequence from position 797-2824 and from position 2180-2606 of SEQ ID NO:1 are SEQ ID NOs:2 and 4, respectively. However, the specification fails to teach the antibodies that bind to polypeptides comprising at least 80% sequence homology to SEQ ID NOs:2, 3 and 4, OR any peptide that has an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2 OR any polypeptide encoded by the nucleotide sequence from position 797-2824 and from position 2180-2606 of SEQ ID NO:1.

Antibodies that bind to the sequences as broadly drawn, read on antibodies that have been subjected to deletions, truncations as well as substitutions. However, the specification has not enabled all of these types of modified proteins because it has not been shown that these modified proteins are capable of functioning as that which is being disclosed.

Eventhough, the claims recite that the protein binds to an N-terminal fragment of plasminogen comprising kringle domain 1-4 and/or 5, there is no guidance as to how to make these divergent sequences, which possess the alleged function. Bork (Genome Research 10:398-400, 2000) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (page 398, column 1). One of the reasons for

the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Bork cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrongly.

Thus, although the specification is enabled for SEQ ID NOs: 2, 3 and 4 in addition to antibodies that binds to such amino acid sequences; the specification does not provide enablement for antibodies that bind to amino acid sequences having at least 80% sequence homology to SEQ ID NOs:2, 3 and 4, OR any peptide that has an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2 OR any polypeptide encoded by the nucleotide sequence from position 797-2824 and from position 2180-2606 of SEQ ID NO:1; because the specification lacks sufficient description for any such proteins or polypeptides.

Further, studies show the binding of an antibody to a protein sequence that is derived from a known protein to which the antibody binds to is unpredictable. For example, Lederman et al (Molecular Immunology 28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). In addition, Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other activities when constructing analogs (see entire document).

Thus, in view of the teachings above, and the lack of guidance and or exemplification in the specification, at the time the application was filed it would not have been predictable for of skill in the art to use the pharmaceutical compositions or

vaccine formulations as contemplated in the disclosure. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Response to Applicants arguments:

The applicants argue (page 10 of the response filed 07/23/2007) that one skilled in the art would be able to make and use antibodies ... because making and identifying variant proteins to a given sequence is routine in the art.

The above arguments are carefully considered but are not found persuasive. The description of the method of assaying for the anti-angiogenic property of an amino acid sequence does not enable a skilled artisan of all the anti-angiogenic peptides having at least 80% sequence identity to SEQ ID NOs:2, 3 or 4, peptides that have an amino acid sequence comprising at least 10 contiguous amino acid residues of SEQ ID NO:2 and amino acid sequences encoded by a nucleic acid molecule that binds under stringent conditions to the nucleotide sequence from position 797-2824 or from position 2180-2606 of SEQ ID NO:1.

> MPEP 2138.04:
> ... conception of a chemical requires both the idea of the structure of the chemical and possession of an operative method of making it). See also Amgen v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (in the isolation of a gene, defining a gene by its principal biological property is not sufficient for conception absent an ability to envision the detailed constitution as well as a method for obtaining it); Fiers v. Revel, 984 F.2d 1164, 1170, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993) ("[b]efore reduction to practice, conception only of a process for making a substance, without conception of a structural or equivalent definition of that substance, can at most constitute a conception of the substance claimed as a process" but cannot constitute conception of the substance; as "conception is not enablement," conception of a purified DNA sequence coding for a specific protein by function and a method for its isolation that could be carried out by one of ordinary skill in the art is not conception of that material).

Thus, the specification does not enable a skilled artisan all the embodiments encompassed within the claims without undue experimentation.

Conclusion

12. Claims 22 and 27 are found allowable.

13. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi
(571) 272-8789

DAVID J. BLANCHARD
~~PATENT~~ PRIMARY EXAMINER